REMARKS

STATUS OF THE CLAIMS

Claims 1-40 and 43-51 are pending as shown in the response filed on July 17, 2006.

PRIORITY

It was again asserted that claims 1-40 and 43-51 are not entitled to priority to any of 09/475,704; 60/114,495; and/or 60/152,195 on the grounds that these applications do not provide written support for SEQ ID NO:30-32. (Office Action, pages 2-3).

Applicants again respectfully disagree with the assertion that the priority applications must set forth the particularly claimed sequences in order to describe these sequences. In fact, while a claim to the benefit of an earlier application requires that the disclosure in the earlier application comply with 35 U.S.C. § 112, first paragraph, compliance with 112, 1st paragraph does not necessarily require that the priority applications set forth *in ipsis verbis* the terms and language recited in the claims. *See, e.g., In re Lukach*, 169 USPQ 795, 796 (CCPA 1971).

SEQ ID NOs:30-32 do not need to appear verbatim in the priority applications in order to meet the requirements of 35 U.S.C. § 112. Here, the skilled artisan would recognize that all three priority applications describe and enable production of synthetic polynucleotide sequences encoding an HIV polymerase (*see, e.g.,* page 4, lines 10-15, page 10, lines 21-26, Example 1 and Section 2.1.2 (starting on page 28) of 09/475,704; page 5, lines 6-14, page 14, lines 5-14; and page 38, lines 4-13 of 60/152,195; and page 36, lines 1-4 of 60/114,495).

Thus, Applicants submit that Applicants are entitled to an effective filing date of the 09/475,704; 60/114,495; and 60/152,195 applications.

CLAIM OBJECTIONS

Applicants again thank the Examiner for the careful attention paid to the claim numbering and acknowledge that because claim 47 depends from dependent claim 2, that the claims will have to renumbered when allowed.

REINSTATED REJECTIONS – CLAIM SCOPE

On page 2 of the Final Office Action, it was noted that the withdrawn rejections under 35 U.S.C. § 112, 1st paragraph were reinstated because of the alleged "breadth of the claims" (Final Office Action, page 2):

> However, upon further consideration of the evidence of record, the 112 first paragraph rejections are reapplied in view of the breadth of the claims. The number of nucleotides in each SEQ ID NO: is at least 2457 nucleotides and thus at least 819 amino acids is encoded by each nucleotide sequence as set forth in SEQ ID NOs:30-32. The total number of 819 amino acid peptides is 1.85×10^{66}. The number of single amino acid substitutions is 15,561. The number of two amino acid substitutions is over 242,000,000. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, *In re Giolito*, 530 F.2d 397, 400, 188 USPQ 645, 648 (CCPA 1976), and that the claims do not commensurate with the guidance provided in the specification.

Applicants again submit that the calculations set forth in the Final Office Action regarding the asserted breadth ignore both structural and functional limitations recited in the claims.

In terms of structure, the claims are drawn to polynucleotides exhibiting at least 90% sequence homology to SEQ ID NO:30-32. Thus, because the number of nucleotides in each of SEQ ID NO:30-32 is at least 2457, the limit on the number of nucleotides that can be changed is 246, which corresponds to, at most, 82 amino acid substitutions in an ~819 amino acid polypeptide (as compared to the polypeptide encoded by SEQ ID NOs:30-32 *per se*). This is nowhere near the 1.85×10^{66} polypeptide variants alleged in the Final Office Action to be covered by the claims.

The Examiner's determination of the breadth of the claims fails to properly consider structural limitations, namely that sequence variation of 90% is determined at the nucleotide (not polypeptide) level, and is, therefore, inaccurate.

Furthermore, the functional limitations recited in the claims have also not been properly taken into account. In this regard, *In re Giolito* was cited for the proposition that "even a single nucleotide or amino acid change can destroy the function of a biomolecule." (Final Office Action, page 2). However, in the pending case, the claims require both 90% identity to the

recited sequences at the nucleotide level and, in addition, that the nucleotide sequence encode an HIV Pol polypeptide that elicits a Pol-specific immune response. Not only is it extremely unlikely that a single amino acid mutation would destroy the recited function of generating a Pol-specific immune response, any polynucleotide that does not elicit a Pol-specific immune response does **not** fall within the scope of the claims. Thus, *In re Giolito* is inapplicable to the pending case.

When all the limitations recited in the claims are properly considered, it is clear that the claims are nowhere near as broad as asserted in the Final Office Action.

35 U.S.C. § 112, 1ST PARAGRAPH, WRITTEN DESCRIPTION

Claims 1-40 and 43-47 were rejected as allegedly not described by the specification as filed. (Final Office Action, pages 2-10). In particular, it was alleged that the written description requirement has not been met because:

(a) the term "an HIV Pol polypeptide that elicits a Pol-specific immune response" is allegedly not defined and that the polypeptide encoded by the claimed polynucleotides must exhibit all native Pol functions (reverse transcriptase activity, integrase activity, etc.);

(b) a "core structure" is not allegedly described; and

(c) the previous evidence of record (PowerPoint slides presented by PTO, PTO Examples regarding written description, Declaratory evidence, and issuance of related patents) does not show that immunogenic activity can tolerate substitutions and is not persuasive because "every case is decided on its own merits [citing *In re Giolito*]." (Final Office Action, page 10).

(a) Definition of "HIV Pol polypeptide that elicits a Pol-specific immune response"

The Final Office Action stated that an HIV Pol polypeptide is one that must have all the Pol activities disclosed in the specification, including RT activity, IN activity, higher protein production and that the term "HIV Pol polypeptide that elicits a Pol-specific immune response" is not defined in the specification. (Final Office Action, page 6, citing page 36 and 73 of the specification).

As a threshold matter, Applicants again submit that the instant claims are not directed to any HIV Pol polypeptide. Rather, as noted above, the claims have been improperly construed to

read out structural (90% sequence identity at the nucleotide level) and functional (the polypeptide encoded the nucleotide elicits a Pol-specific immune response) limitations. The polypeptide is not required to have all Pol activities – eliciting a Pol-specific immune response is sufficient.

Moreover, the term "immunogenic HIV polypeptide" is defined throughout the specification to refer only to HIV Pol polypeptides that elicit an immune response. *See, e.g.,* page 17, lines 1-6, where it is plainly noted that an immunogenic polypeptide is one which elicits a humoral and/or cellular immune response "to the antigenic molecule of interest," in this case a immune response to HIV Pol (emphasis added):

> An "immunogenic composition" is a composition that comprises an antigenic molecule where administration of the composition to a subject results in the development in the subject of a humoral and/or cellular immune response to the antigenic molecule of interest.

See, also, pages 36 and 73 of the specification as cited in the Office Action, which unambiguously indicates that HIV Pol polypeptides encoded by the claimed sequences can lack enzymatic function but still retain their Pol-specific immunogenicity. This clearly contradicts the assertion that HIV Pol polypeptides must exhibit RT and INT enzymatic activity.

In addition to the fact that the specification clearly teaches that the polypeptide encoded by the claimed sequences elicits a Pol-specific immune response, Applicants believe that reading "immune response" out of the context with "HIV Pol-specific" renders the claim meaningless and fails to comport with the knowledge of one of skill in the art in the field of HIV and molecular biology.

It was also well known at the time of filing that an HIV Pol polypeptide would elicit an immune response specific for HIV Pol, even when the Pol polypeptide did not exhibit "other" Pol functions. *See, e.g.,* WO 00/39302 (Ref B93 of IDS filed December 18, 2002 and considered February 21, 2003). Therefore, in light of the art, as exemplified by the references discussed above, the term "HIV Pol polypeptide that elicits a Pol-specific immune response" cannot be construed to encompass polypeptides that do not induce a Pol-specific response (*e.g.,* polypeptides that induce general, non-Pol-specific immune responses).

Indeed, the importance of construing claim language in light of the art was recently reaffirmed by the Federal Circuit, *en banc*, in *Phillips v. AWH*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005). Therein, the court, citing a number of previous decisions,[1] confirmed its precedent that claim terms are given their ordinary and customary meaning to a person of ordinary skill in the art at the effective filing date of the patent application (*Phillips v. AWH Corp.*, 75 USPQ2d 1321, 1326 (Fed. Cir. 2005)):

> We have made clear, moreover, that the ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application.

At the time of filing, the skilled artisan was well aware at that date, an "HIV Pol polypeptide that elicits a Pol-specific immune response" would not include polypeptides that did not elicit Pol-specific immune responses.

Thus, the meaning attributed by the Examiner to the term "HIV Pol polypeptide that elicits a Pol-specific immune response" is not the meaning of that term as set forth in the specification or the meaning of the term to one of skill in the relevant art. To assert that the term "HIV Pol polypeptide that elicits a Pol-specific immune response" is not defined and/or does not limit the scope of the claims on the grounds that all Pol activities (enzymatic, immunogenic or otherwise) must be exhibited, stretches the meaning of the claims beyond credulity. The skilled artisan would clearly know the definition of the term an "HIV Pol polypeptide that elicits a Pol-specific immune response" based on the specification as-filed and the state of the art at the time of filing. Accordingly, the scope of the claims is also clearly defined.

The claimed sequences encode polypeptides that elicit specific (HIV Pol) immune responses and sequences that do not encode polypeptides that produce an HIV Pol-specific immune response are not encompassed by the pending claims. In other words, the genus encompassed by the claims is nowhere near as broad as that painted in the Final Office Action. When the claims are properly construed, it is plain that they are drawn to a genus of nucleotide

[1] See, for example, *Veronicas Corp. v. Conception, Inc.* 90 F.3d 1576, 1582 (Fed. Cir. 1996); *Ferguson Beauregard/Logic Controls v. Mega Sys., LLC*, 350 F.3d 1327, 1338 (Fed. Cir. 2003) and *Home Diagnostics, Inc. v. Life Scan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004)

sequences encompasses only those nucleotide sequences that encode a polypeptide that elicits a humoral and/or cellular immune response specific for an HIV Pol polypeptide.

(b) The Evidence of Record Establishes that A "Core Structure" Does Not Need to be Described

The Final Office Action has also alleged that adequate written description of a nucleotide sequence requires that the specification describe "which nucleotides are considered essential for eliciting a humoral and/or cellular immune response."[2] (Final Office Action, page 6). In addition, the Final Office Action also states that the evidence of record, does not support the assertion that a protein can tolerate multiple substitutions and still remain its immunogenic function. (Final Office Action, page 10).

Applicants submit that there is ample evidence of record establishing that "essential nucleotides" for eliciting an immune response do not need to be listed to meet the written description requirement. Furthermore, this evidence also establishes that the structure of immunogenic HIV Pol polypeptides were known and that these polypeptides can tolerate many substitutions and still retain immunogenic function.

It is axiomatic that a specification need not re-describe known molecules in order to satisfy the written description requirement. See, *Spectra-Physics, Inc. v. Coherent, Inc.* 3 USPQ2d 1737, 1743 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986). Recently, the Federal Circuit in *Falkner v. Inglis,* 79 USPQ2d 1001 (Fed. Cir. 2006), reaffirmed that adequate written description does not require re-description of the sequence of known molecules and that literature available at the time of filing must be considered in determining the adequacy of the written description (*Falkner*, page 1007-1008, emphasis added):

> Specifically, we hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and **(3) there is no *per se* rule that an**

[2] Applicants note that nucleotides are not responsible for immunogenicity. Rather, it is the polypeptide as a whole encoded by a particular sequence of nucleotides that elicits the immune response.

adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.

> Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. As we stated in Capon, "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." Id. at 1358. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (wherein permitted) of such genes and sequences.

In the instant case, Applicants are not required to re-describe the sequences of known immunogenic HIV Pol polypeptides in order to satisfy the written description requirement. The claims are directed to novel polynucleotides that encode immunogenic HIV Pol polypeptides. At the time of filing (and indeed to this day), the structure (primary and secondary) of immunogenic HIV Pol polypeptides was well-known to the skilled artisan.

Nor are Applicants required to describe "essential" residues relating to the claimed function of immunogenicity. In fact, the evidence of record clearly establishes that there is not one core structure responsible for immunogenic function. Rather, an HIV Pol polypeptide can tolerate many mutations and still generate a Pol-specific immune response. Production of an immune response to an antigen is routinely practiced in the absence of knowledge of a protein's primary or tertiary structure. *See, also,* page 14, lines 19-29 of the as-filed specification regarding epitopes. Indeed, as acknowledged in the Final Office Action, the specification itself teaches that altering the claimed polynucleotide such that the HIV Pol protein it encodes loses RT and/or INT activity but is produced at high levels and retains Pol-specific immune activity. *See, e.g.,* Table B on page 35 and text on pages 35-36; page 73.

See, also, Declaration of Dr. Donnelly, filed December 27, 2002, establishing that it was well-known to the skilled artisan at the time of filing that immunogenicity of HIV Gag polypeptides does not correlate with a core structure (Declaration, ¶18, emphasis added)[3]:

> 17. Second, at the time the specification was filed, it would have been clear to a typical scientist that the inventors' specification fully described and contemplated that the claimed polynucleotides encoded immunogenic Pol polypeptides. Methods of testing Pol immunogenicity were well-known at the time of filing and are demonstrated, for example, in Exhibit B. Indeed, our experiments, presented in Exhibit B, indicate that Pol-specific immune responses are generated to the claimed sequences. In sum, based on the disclosure of the specification and the level of knowledge of a typical scientist regarding sequence identity, and testing for immunogenicity, I believe that the specification as filed clearly conveys that the applicants had invented the expression cassettes as set forth in the claims.

Further, as noted in the last response, the Office has admitted on the record that it is well known that the immunogenic function of a polypeptide can tolerate many modifications and that the structure of an HIV Pol is well known (see, pages 22-23 of Office Action mailed on August 9, 2005 in which the Office stated on the record that the §112, 1st paragraph (written description and enablement) rejections were withdrawn, emphasis added):

> Applicant's arguments, see pages 8-11, filed 5/16/05, with respect to 112 first paragraph written description have been fully considered and are persuasive. The rejection of claims 1-40 and 47 has been withdrawn because **the instant polynucleotide sequences recite a structure and function and that function can tolerate many modifications and the structure of an HIV Pol is well known in the prior art as stated in the Declaration filed by Dr. Donnelly filed 9/8/03.**
>
> Applicant's arguments, see pages 8-11, filed 5/16/05, with respect to 112 first paragraph enablement have been fully considered and are persuasive. The rejection of claims 1-40 and 47 has been withdrawn because **several polynucleotide sequences comprising a nucleotide sequence encoding an HIV Pol polypeptide were well known in the art at the time the invention was**

[3] The Declaration of Dr. Donnelly has not been adequately considered. In point of fact, this declarations further establishes that the sequences having at least 90% identity to SEQ ID Nos:30-32 are both enabled and described by the as-filed specification. Using specific facts, Dr. Donnelly concludes that the as-filed specification describes and enables the claimed subject matter. This convincing, factual evidence has been improperly dismissed by the Office (see, e.g., In re Alton, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

> **made** (See, U.S. Patent No. 6,602,705 and prior art rejections of record and the skilled artisan can make a sufficient number of species to represent the genus of polynucleotide sequences (See Declarations of Record, filed 9/8/03 and 12/27/02).

See, also, page 5 of the Office Action mailed February 15, 2006 acknowledging that

> [t]he specification contemplates production of a genus of a polynucleotide sequence encoding an immunogenic HIV [Pol] polypeptide, wherein the polynucleotide sequence encoding said Pol polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO:30, 31 or 32. The as-filed specification provides sufficient description of an immunogenic HIV Pol polypeptide as set forth in SEQ ID NO:30, 31, or 32.

Therefore, as repeatedly acknowledged by the Office, the written description requirement is satisfied with respect to the genus of polynucleotides as claimed. Not only is a core structure not describable for immunogenic HIV Pol polypeptides, it has been acknowledged that the evidence of record clearly supports that the written description requirement in the instant case does not necessitate that Applicants re-describe known immunogenic HIV Pol polypeptides that are encoded by their novel polynucleotides or set forth epitopes of these encoded polypeptides in the claims. *See*, specification, *e.g.*, Examples and supporting post-filing date published data submitted with Donnelly Declarations.

(c) The Evidence of Record Establishes that Written Description is Satisfied in the Pending Case

The Final Office Action also stated that other evidence of record, including recent Federal Circuit case law regarding written description, PTO presentations and PTO Guidelines, is irrelevant because "each case is decided on it's own merits." (Final Office Action, page 10). Paradoxically, the Final Office Action cites *In re Giolito*, a 30-year old CCPA case, in support of the position that this evidence can be ignored. (Final Office Action, page 10).

Applicants submit that, based on the particular facts in this case (including disclosure, common knowledge and evidence of record), the written description requirement has in fact been more than amply satisfied in the instant case.

Legally, the amount or nature of any testing is not a factor considered in assessing the adequacy of description. *See, e.g., Capon v. Eshhar,* 76 USPQ2d 1078, 1085-1086 (Fed. Cir. 2005):

> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. ...
>
> Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. [citations omitted].
>
> It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. See In re Angstadt, 537 F.2d 498, 504 [190 USPQ 214] (CCPA 1976) ("The examples, both operative and inoperative, are the best guidance this art permits, as far as we can conclude from the record"). While the Board is correct that a generic invention requires adequate support, the sufficiency of the support must be determined in the particular case. Both Eshhar and Capon present not only general teachings of how to select and recombine the DNA, but also specific examples of the production of specified chimeric genes.
>
> The PTO points out that for biochemical processes relating to gene modification, protein expression, and immune response, success is not assured. However, generic inventions are not thereby invalid.

Capon also reiterates that well-settled notion that description of a single species can provide an adequate description, even for a broad genus. A specification need not describe every polynucleotide permutation in order for an inventor to obtain a generic claim and actual reduction to practice of polynucleotides falling within the scope of the claims is never necessary for compliance with the written description requirement.[4] Description does not require exemplification. *See, Capon v. Eshhar* 76 USPQ2d 1078 (CA FC 2005):

[4] *See, also,*, the PTO Guidelines, favorably commented on by the Federal Circuit, include various Examples that establish that claims to a genus of sequences are properly described if (1) the DNA sequence is novel, (2) unobvious, and (3) a specific activity is recited. *See,* Examples 9 and 14 of the PTO Guidelines on Written Description, reproduced in the Response filed September 26, 2005.

> It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. *See In re Angstadt*, 537 F.2d 498, 504 [190 USPQ 214] (CCPA 1976) ("The examples, both operative and inoperative, are the best guidance this art permits, as far as we can conclude from the record"). While the Board is correct that a generic invention requires adequate support, the sufficiency of the support must be determined in the particular case. ...

See, also, Falkner v. Inglis, in which the Federal Circuit cited *Capon* in reiterating that actual reduction to practice is not required (*Falkner,* at 1007-1008):

> Specifically, we hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description **(2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent**; and (3) there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure. ...
>
> As we explained in *Capon v. Eshhar*, "[t]he 'written description' requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed." 418 F.3d 1349, 1357 [76 USPQ2d 1078] (Fed. Cir. 2005). ....
>
> Thus, to the extent that written description requires a showing of "possession of the invention," *Capon*, 418 F.3d at 1357 (emphasis added), [it is] clear that **an invention can be "complete" even where an actual reduction to practice is absent**.

These clear, fact-independent holdings of the Federal Circuit are applicable to every written description inquiry, including the instant case and, accordingly, cannot be dismissed on the grounds that each case is decided on its own merits. By this criteria, no case law would be relevant, including the cases cited in the Final Office Action.

In addition to the applicable Federal Circuit case law of record, Applicants submit that the particular disclosure and additional declaratory and published evidence of the instant case also plainly support a finding that the written description requirement is satisfied.

The as-filed specification contains ample disclosure including exemplification of sequences comprising the claimed reference sequence that encode immunogenic HIV Pol

polypeptides. In fact, the exact sequence of reference sequences SEQ ID NOs:30-32 are literally described in the as-filed specification. Therefore, it is clear that Applicants were in possession of not only these molecules but, in addition, nucleotides exhibiting 90% identity to these molecules.

Furthermore, regardless of the number of variants encompassed by the claims, Applicants reiterate that the as-filed specification teaches, in detail and with working examples, how to obtain the claimed polynucleotides. Each and every member of the claimed genus – be it 2 or 2 billion members in size – is **literally** described in the as-filed specification. Satisfaction of the written description requirement does not necessitate that each and every member of the claimed genus be set forth, let alone "tested" in order to show possession. Nor does the written description requirement necessitate a showing that the skilled artisan can predict *a priori* each and every nucleotide sequence falling within the scope of the claims. Even if it did, Applicants have met this inasmuch as the as-filed specification contains unambiguous **literal** description of the structure of any member of the claimed genus by reference to its sequence similarity to a reference sequence.

Thus, the process for testing the polypeptides encoded by the claimed sequences is much more than possible, it is amply described in sufficient detail to demonstrate that Applicants were in possession, at time of filing, of any nucleotide sequence that exhibits 90% identity to SEQ ID NOs:30-32 and which encodes an HIV Pol polypeptide that elicits an Pol-specific immune response in a subject.

Furthermore, as discussed above, Dr. Donnelly's Declaration (including a published journal article) also demonstrates that, based on the particular facts of this case, a written description rejection is untenable. Indeed, the Office has admitted on the record that the specification and this Declaration establish that "the instant polynucleotide sequences recite a structure and function and that function can tolerate many modifications and the structure of an HIV Pol is well known in the prior art as stated in the Declaration filed by Dr. Donnelly filed 9/8/03." (Office Action mailed August 9, 2005, pages 22-23).

The test for determining satisfaction of the requirement of Section 112, 1st paragraph is not what sequences are actually reduced to practice in the as-filed specification, but, rather, what the disclosure as a whole and available knowledge to determine whether the specification as-

filed evinces possession of the claimed subject matter to the skilled artisan. The skilled artisan, having followed the teaching of the specification, would have no doubts that Applicants were in possession of the claimed subject matter (and that the as-filed specification teaches how to make and use the claimed sequences).

Therefore, for the reasons of record and those set forth herein, the as-filed specification more than satisfies the written description requirement of 35 U.S.C. § 112, 1st paragraph.

35 U.S.C. § 112, 1ST PARAGRAPH, ENABLEMENT

Claims 1-40 and 43-47 were also again rejected under 35 U.S.C. § 112, 1st paragraph as allegedly not enabled by the as-filed specification. (Final Office Action, pages 11-16).

As set forth in the seminal case of *In re Marzocchi,* 439 F.2d, 220, 223, 169 USPQ 367, 369 (CCPA 1971), a patent application is presumptively enabled when filed:

> [a]s a matter of Patent Office practice ... a specification .. must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Moreover,

> it is incumbent upon the Patent Office, whenever a rejection on [grounds of enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

439 F.2d at 224, 169 USPQ at 369-370. Indeed, as pointed in the Patent Office's own Training Manual on Enablement (1993, citing *In re Wright,* 999 F.2d 1557, 1561-1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993), "the case law makes clear that properly reasoned and supported statements explaining any failure to comply with section 112 are a requirement to support a rejection."

In the pending case, the enablement rejection is allegedly supported by citing Baker, Attwood, Gerhold, Russel, Wells and Ngo, which were alleged to demonstrate the unpredictability of "the relationship between sequence and function" (Final Office Action, page

13). However, these references do not provide a properly reasoned and supported basis for finding non-enablement.

Baker, Attwood, Russell and Ngo are cited for allegedly showing unpredictability of the relationship of primary, secondary and tertiary structure of a polypeptide. However, as noted above, the evidence of record establishes a Pol-specific immune response can be generated by short epitopes and, accordingly, there is no need to predict, a priori, the "structure" or "folding" of a polypeptide encoded by the claimed molecules.

Likewise, Gerhold and Wells relate to methods of determining gene function based on EST sequence. This is not relevant to the pending claims, in which the only function required by the polypeptide is that elicits a Pol-specific immune response and which required function does not necessitate the entire coding sequence or core structures.

The relevant question regarding enablement remains what the specification and state of the art at the time of filing teaches one of skill in the art in regard to eliciting Pol-specific immune responses. The disclosures of Baker, Attwood, Gerhold, Russel, Wells and Ngo do not change the fact that any experimentation needed to polynucleotides exhibiting 90% sequence identity to SEQ ID NOs:30-32 and which encode an immunogenic Pol polypeptide is utterly routine in view of the teachings of the specification and the state of the art. The Office has not provided sufficient evidence supporting non-enablement and, in the absence of necessary relevant evidence contradicting the teachings of the specification and state of the art, the rejection cannot be maintained.

(a) Undue Experimentation is Not Required to Make and Use the Claimed Polynucleotides

Applicants also remind the Office that it is well settled that even time-consuming or expensive experimentation is **not** undue if it is routine. (See, *e.g.*, PTO Training Manual on Enablement, pages 30-31, citing *United States v. Electronics Inc.*, USPQ2d 1217, 1223 (Fed. Cir. 1988), *cert. denied* 490 U.S. 1046 (1989) holding the disclosure of a single exemplified embodiment and a method to determine other embodiments was enabling, even in the face of evidence that determining additional embodiments might require 6-12 months of effort and cost over $50,000). Furthermore, the notion that one of ordinary skill in the art must have reasonable

assurance of obtaining an active claimed product has been emphatically rejected by the courts. *See, Angstadt* at 219. So long as it is clear that some species render a composition operative, the inclusion of some possible inoperative species does not invalidate the claim under paragraph 1, of 35 U.S.C. §112. *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, CCPA 1971; *Horton v. Stevens*, 7 USPQ2d 1245, 1247, Fed. Cir. 1988.

At the time of filing, the state of the art was such that a skilled artisan could routinely produce antibodies that specifically bind to a protein by immunizing an appropriate host with oligopeptide fragments of that protein. It was well known in the art that it was possible to produce antibodies to almost any part of an antigen, and was not especially difficult to obtain antibodies with specificity for a particular protein, as set forth in the claims. Moreover, a specific cellular immune response is also routinely produced by immunization with antigen.

The specification also provides ample guidance for one of skill in the art to elicit an immune response (*i.e.*, humoral and/or cellular) with the recited polynucleotides encoding HIV Pol polypeptides that elicit a Pol-specific immune response, disclosing, *e.g.*, the precise sequence of the reference sequences, how to determine sequences having 90% identity to these reference sequences, how to express a polypeptide from the polynucleotides having the requisite sequence homology, and how to test these sequences of their ability to elicit a Pol-specific immune response.

The actual scope of the claims, and the nature of the guidance provided in the specification (*e.g.*, at Examples), along with the conventional nature of methods of modifying sequences and determining their function, all establish that the specification as filed fully enables the claims.

Moreover, the state of the art and clear teachings of the specification are supplemented by further evidence (Declaration, post-filing date publications, etc.) of the routine nature of making and using the claimed polynucleotides. Applicants are not required to show perfect efficiency or success rates. All that is required is that one of skill in the art could make and use the claimed polynucleotides. The specification and evidence of record plainly demonstrate that this requirement has been met.

In sum, given the clear teachings in the specification and the high level of knowledge at the time of filing, it would not require undue experimentation to make and use polynucleotides as

claimed. Furthermore, for the reasons of record and reiterated above, the references cited by the Office do not provide any reasons to doubt that the skilled artisan could make and use the claimed molecules.

Thus, for the reasons of record and above, the specification describes and enables the claimed subject matter. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, are respectfully requested.

PROVISIONAL OBVIOUSNESS-TYPE DOUBLE PATENTING

Applicants request the provisional double patenting rejection over 10/190,435 be held in abeyance until indication as at allowable claims is received in one of the applications.

CONCLUSION

In view of the foregoing amendments, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §1.16, §1.17, and §1.21, which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648, referencing Atty. Docket No. 2302-1631.20.

Please direct all further written communications regarding this application to:

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Respectfully submitted,

Date: March 5, 2007

By: _____

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